## REMARKS

Claims 1, 14 and 23 are pending. New claim 23 has been added. Claims 2-13 and 15 to 22 have been cancelled without prejudice or disclaimer. Claim 1 has been amended to additionally incorporate therein the subject matter of former claims 2, 8 and 10. Claim 14 has been amended to recite only compounds 6a – 6e. New claim 23 has been added, which is supported by compounds 6c – 6e, as set forth in for example Figure 2. Applicants reserve the right to pursue any subject matter removed by these amendments in one or more divisional and/or continuation applications. For the reasons outlined below, the rejections set forth in the Office Action of June 21, 2002 are respectfully traversed and reconsideration and withdrawal are respectfully requested.

### Election/Restrictions and Claim Objections

The Examiner has acknowledged the election, with traverse, of the claims of group I (claims 1-14); of thioether as the substituent; and of alkyl as group "X", as per applicants' letter of April 18, 2002 (Paper No. 11). Solely to advance prosecution, claims 1-14 have been amended (see above) so that they do not read on non-elected embodiments, as per the Examiner's request.

### Specification

The title and abstract have been amended as per the Examiner's request.

### Claim Rejections – 35 USC § 112

Claims 1-14 are rejected pursuant to 35 USC § 112, first paragraph, on the grounds that the specification does not provide a written description commensurate in scope with the claims.

Solely in order to advance prosecution, claim 1 has been amended to recite a C8-substituted adenine nucleotide, wherein the adenine nucleotide is substituted at the C8 position with a thioether substituent, wherein the thioether substituent has the structure:

-S-X ;

wherein X is selected from the group consisting of:

(a) $C_7H_{13}$ (cycloheptyl)

(b) $(CH_3)_3CCH_2$; and

(c) $CH_3(CH_2)_n$, wherein $1 \leq n \leq 5$.

Claims 14 and 23 depend from claim 1 and include the limitations thereof.



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Applicant respectfully submits that the instant specification provides a complete written description of the subject matter of the claims as presently amended. Indeed, most of the presently claimed subject matter is described in working examples in the application as discussed herein. Adenine nucleotides having the substituents (a) and (b) of amended claim 1 are supported by compounds 6a and 6b as set forth in Figure 2 of the application. (c) of this group is supported by compounds 6c to 6e as set forth in Figure 2 of the application. Regarding the latter, applicant respectfully submits that the working examples in the specification (including compounds 6c, 6e and 6d, wherein n = 1, 3 and 5, respectively) provide a written description of the claimed genus recited in (c) of claim 1. In light of the above, applicant respectfully submits that the specification provides a written description of the presently claimed subject matter and respectfully requests reconsideration and that the rejection be withdrawn.

Further, new claim 23 has been added which is directed to the embodiments wherein n is selected from 1, 3 and 5 as specifically exemplified in the working examples in the specification.

Claims 1-14 are rejected pursuant to 35 USC § 112, first paragraph, as allegedly lacking enablement. Applicant first respectfully submits that the claims as amended are fully enabled by the specification. The claims as presently amended are directed to compounds whose utility is exemplified by the representative working examples set forth in the specification. Further, the claims as amended are directed to C8-substituted adenine nucleotides where the substituent is selected among particular thioethers, the preparation of which is described in the working examples in the specification.

The Examiner has further commented with respect to [$Sar^9$, $Met(O_2)^{11}$]SP (NK-1), utilized in Example 2. Applicant notes that NK-1 is a commercially available reagent available from e.g. from Sigma-Aldrich under product no. S-3672 (copy of catalog excerpt attached). Those of ordinary skill in the art would immediately recognize that NK-1 from a commercial source could be substituted for that described in the instant specification. In light of the above, applicant respectfully requests reconsideration and that the rejection be withdrawn.

Claim Rejections – 35 USC § 102(e)

Claims 1-14 are rejected pursuant to 35 USC § 102(e) as being anticipatedby US Patent 6,312,662 to Erion et al, based on contention that Erion et al. disclose a C8-thioalkyl purine.



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Applicants respectfully traverse this rejection. Faced with the disclosure of the '662 patent, applicants respectfully submit that one of ordinary skill in the art would not be able to "at once envisage" the compounds as presently claimed, as required for a finding of anticipation. See *Ex parte A*, 17 USPQ2d 1716. Similarly, the recitation in the '662 patent of the generic term "8-thioalkyl ... purine" does not "describe" and therefore does not anticipate the compounds as presently claimed. See *In re Petering*, 133 USPQ 275. In light of the above, applicants respectfully submit that the claims as amended are novel over the '662 patent and therefore reconsideration and withdrawal of the rejection of the claims under 35 USC §102(e) over the '662 patent are respectfully requested.

Attached hereto is a marked-up version of the changes made to the specification by the current amendment. The attachment is captioned "Version with markings to show changes made."

It is believed this responds to all of the Examiner's concerns, however if the Examiner has any further questions, he is invited to contact David Schwartz (Reg. No. 48,211) at 613-232-2486.

Applicant respectfully requests that a timely Notice of Allowance be issued in this case.

Respectfully submitted,

Nicholas J. Seay
Reg. No. 27,386
Attorney for Applicant
QUARLES & BRADY LLP
PO Box 2113
Madison, WI 53701-2113

TEL 608/251-5000
FAX 608/251-9166

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

Applicants: Adrien R. Beaudoin
Fernand-Pierre Gendron
Effrat Halbfinger
Bilha Fischer

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Examiner: Bradley L. Sisson

Title: C8-SUBSTITUTED PURINE NUCLEOTIDE ANALOGS AND THEIR USE AS INHIBITORS OF NUCLEOSIDE TRIPHOSPHATE DIPHOSPHODYROLASES

File No.: 850865.90015



In the Title:

Please amend the title on page 1, and please update the Patent Office records, so that the title reads as follows:

C8-SUBSTITUTED PURINE NUCLEOTIDE ANALOGS [AND THEIR USE AS INHIBITORS OF NUCLEOSIDE TRIPHOSPHATE DIPHOSPHOHYDROLASES]

In the Claims:

Please cancel Claims 2 to 13 and 15 to 22, amend Claims 1 and 14, and add new Claim 23 as follows:

1. A C8-substituted [purine] adenine nucleotide, wherein the [purine] adenine nucleotide is substituted at the C8 position with a thioether substituent [other than H], wherein the thioether substituent has the structure:

-S-X ;

wherein X is selected from the group consisting of:

(a) $C_7H_{13}$ (cycloheptyl)

(b) $(CH_3)_3CCH_2$; and

(c) $CH_3(CH_2)_n$, wherein $1 \leq n \leq 5$.

14. The [purine] adenine nucleotide of claim 1 selected from the group consisting of[:]



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compound **6a**, compound **6b**, compound **6c**, compound **6d**, and compound **6e**[, compound **7a**, compound **7b**, compound **7c**, compound **7d**, compound **7e**, compound **8a**, compound **8b**, compound **8c**, compound **8d**, and compound **8e**].

23. The adenine nucleotide of claim 1, wherein n is selected from the group consisting of 1, 3 and 5.

In the Abstract:

Please amend the Abstract to read as follows:

ABSTRACT

[Ectonucleoside triphosphate diphosphohydrolases [NTPDases; EC 3.6.1.5] constitute a family of enzymes which are involved in the metabolism of extracellular nucleotides, catalysing the hydrolysis of the gamma and beta phosphate bonds of triphospho- and diphosphonucleosides (whereas 5'nucleotidases [EC 3.1.3.5] catalyse the hydrolysis of alpha phosphate bond of monophosphonucleosides). These extracellular nucleotides interact with endothelial, epithelial and smooth muscle cells, as well as blood cells and lymphoid cells, to influence the different physiological systems of vertebrates. Since these ecto-nucleotidases alter the extracellular concentrations of nucleotides these enzymes modulate their physiological effects, including, for example, platelet aggregation, heart function, control of vascular tone and inflammation reactions, electrolyte secretion and gastrointestinal motility, neurotransmission both in central and peripheral nervous systems, as well as other effects in other physiological systems. This invention provides C8 substituted purine nucleotide analogues, such as ATP analogues, and further provides their use as inhibitors of NTPDases and thereby as tools to modulate the conversion of nucleotides into nucleoside derivatives, and thus modulate the levels of these compounds. Such modulation further provides for the modulation of the activity and function of many processes which are affected by these compounds.] C8-substituted purine nucleotide analogs, such as ATP analogs, and their use is described, including their use as inhibitors of NTPDases and thereby as tools to modulate the conversion of nucleotides into nucleoside derivatives, and thus modulate the levels of these compounds. Such modulation further provides for the modulation of the activity and function of many processes which are affected by these compounds.



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